Amendments to the Claims

Claim 1 was amended to recite "a translocation domain comprising an amino acid sequence at least 60% identical to a sequence of PE domain II and capable of effecting translocation to a cell cytosol." Support for the "at least 60%" subject matter is found at p. 27, first two lines, which provides for a translocation domain which is "substantially identical" to that of PE domain II and the first full paragraph at p. 16., which defines what is meant by the phrase "substantially identical." Support for the "capable of effecting translocation" subject matter is found, *inter alia,* at p. 32, lines 20-30 and also in the previous language of the claim which recited "sufficient to effect translocation."

Claim 1 was further amended to recite "an epitope presenting domain located at the PE Ib domain location of PE and having one cysteine to cysteine disulfide bonded loop and comprising an amino acid sequence of between 5 and 350 amino acids that encodes an epitope that is non-native to PE domain Ib and is located within the loop, and wherein the epitope is from a pathogen."

Support for the "located at the PE Ib domain location of PE" subject matter is found *inter alia* in the paragraph bridging pp. 27 and 28.

Support for the subject matter of an epitope located within the one cysteine-cysteine loop is set forth, *inter alia,* at p. 28, line 13 - page 29 line 3 and illustrated in Figures 1A and 1B.

Support for the subject matter of "an amino acid sequence of between 5 and 350 amino acids that encodes an epitope" is found in the specification at p. 30, lines 18-22, which provides ranges of "between about 5 and 1500 amino acids", "between about 15 and 350 amino acids", and "between about 15 and 50 amino acids." With respect to the subject matter in the range of 5 to 15 amino acids, the specification additionally has examples of domains having at least 8 amino acids (p. 32, line 15) and of 14 amino acids (p.47, line 16).

Support for the "epitope non-native to PE domain Ib" subject matter is found in the specification at p. 23, lines 4 and 5.

Support for the subject matter of "wherein the epitope is from a pathogen" is found throughout the specification. For instance, see page 29, line 14.

As Applicant believes the proposed amendments to the claims add no new matter, Applicant respectfully requests their entry.

## RESPONSES TO THE REJECTIONS

### A. Response to the Rejection of Claim 8 as being allegedly indefinite.

Claim 8 recites:

> "The immunogen of claim 1 wherein the translocation domain is domain II of PE."

In order to expedite prosecution of the application and without acquiescing to the position of the Examiner, Applicant has amended claim 1 as follows:

> a translocation domain comprising an amino acid sequence [substantially] at least 60% identical to a sequence of PE domain II;

In view of the above amendment that specifies the percent sequence identity[1], Applicant submit that a translocation domain of PE having 100% identity with domain II of PE falls within the subject matter of a " a translocation domain comprising an amino acid sequence at least 60% identical to a sequence of PE domain II."

Applicant therefore respectfully requests that the above rejection be reconsidered and withdrawn.

### B. Response to the Rejection of Claim 9 for Alleged Indefiniteness.

Applicant canceled claim 9 in the last amendment, but had failed to so point out in the introductory Remarks. Applicant herein affirms the cancellation of claim 9.

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[1] Support for the amendment is as described above. Enablement of the subject matter is supported by the specification which teaches that the translocation domain may be extensively reengineered at pp. 26-27 and still retain its activity. For instance, this section teaches that a translocation domain with only about 57% sequence identity to that of PE domain II is active (i.e., a translocation domain having amino acids 253-279 (a stretch of 26 amino acids) and 345-366 (a stretch of 21 amino acids) can be eliminated from domain II

**C. Response to Rejection of Claims 1-3, 7-9, 12-13, 24-25 and 44-45 under 35 U.S.C. §112, first paragraph, for an alleged failure to meet the written description requirement.**

In order to expedite prosecution of the application and without acquiescing to the position of the Examiner, Applicant has amended claim 1 to recite "an epitope presenting domain located at the PE Ib domain location of PE" in place of the offending recital of "in between the translocation domain and ER retention domain." Applicant believes the amendment fully addresses the concern identified by the Examiner and respectfully requests reconsideration.

**D. Response to Rejection of Claims 1-3, 7-9, 11-12, 24-25, and 44-45 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness.**

Applicant has amended claim 1 to recite:

> 4) an epitope presenting domain located at the PE Ib domain location of PE and having one cysteine to cysteine disulfide bonded loop and comprising an amino acid sequence of between 5 and 350 amino acids that encodes an epitope that is non-native to PE domain Ib and is located within the loop.

This recital makes clear that the cysteine-cysteine loop of the epitope presenting domain is in place of the cysteine-cysteine bridge of the native Ib domain.

In view of the above amendment, Applicant respectfully requests that the above rejection be reconsidered and withdrawn.

**E. Response to Rejection of Claims 24 and 25 for alleged double-patenting.**

In order to expedite the present application and without acquiescing to the position of the Examiner, Applicant has canceled claims 24 and 25 and claims 44 and 45 which depend from them. These amendments render the issue moot.

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(which altogether has about 111 amino acids) and retain its biological activity (see p. 27, first full paragraph).

## CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 925-472-5000.

Respectfully submitted,

Frank J. Mycroft
Reg. No. 46,946

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
FJM:mmm
WC 9053032 v2

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claims 1, as follows:

1. (Twice Amended) A non-toxic *Pseudomonas* exotoxin A-like ("PE-like") chimeric immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface receptor; (2) a translocation domain comprising an amino acid sequence [substantially] at least 60% identical to a sequence of PE domain II and capable of effecting [sufficient to effect] translocation to a cell cytosol; (3) an amino acid sequence encoding an endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence[,]; (4) an epitope presenting domain located at the PE Ib domain location of PE and having one cysteine to cysteine disulfide bonded loop [in between the translocation domain and ER retention domain] and comprising [(i)] an amino acid sequence of between 5 and 350 amino acids that encodes an epitope that is non-native to PE domain Ib and is located within the loop, and wherein the epitope is from a pathogen. [and (ii) two cysteine residues native to PE that form a cysteine-cysteine disulfide bonded loop, wherein the epitope is inserted in between the two cysteine residues.]